REMARKS

This Reply is submitted in response to the Final Action dated June 4, 2004. Applicants request respectfully that the Examiner enter the proposed amendments and reconsider the patentability of the claimed invention. The amendments are believed to comply with MPEP § 714.12 in that they place the claims in better form for appeal, do not increase the number of pending claims, and do not require additional searching.

Status of the Claims

The Examiner's Action addresses all of applicants' elected claims, namely claims 1, 3 to 39, 41, 42, 47 and 49 to 66. The amendment of Claims 1, 4, 41,47, 64 and 65 is requested. No claims have been added or cancelled. Accordingly, claims 1, 3 to 39, 41, 42, 47 and 49 to 66 are presented for the Examiner's consideration.

The requested amendment of claim 1 converts the claim to the form in which it was filed originally. The claim definitively and unambiguously defines a dosage form which is a solid and which includes a solid composition, all the ingredients of which are solids at room temperature.

Editorial amendments have been made to claims 4, 41, 47, 64, and 65.

Introduction and Summary of the Examiner's Rejections

As set forth in the previous Reply, filed February 23, 2004, applicants' claims define two embodiments, namely the "all solids" embodiment, as defined independent claims 1 and 41 and the "fatty acid compound enhancer" embodiment, as defined in independent claims 53, 64, and 65.

With respect to the "all solids" embodiment, the Examiner has reasserted the §102 rejection of claims 1, 3 to 13, 15 to 39, 41, 42, 47 and 49 to 52 based on the disclosure of Published International Application No. WO 97/05903, inventors Watts et. al (hereafter "the Watts publication") and has reasserted also the §103 rejection of claims 1, 3 to 39, 41, 42, 47, and 49 to 52 based on disclosure of the Watts publication.

With respect to the "fatty acid compound enhancer" embodiment, the Examiner has reasserted his §103 rejection of claims 53 to 66 based also on the disclosure of the Watts publication in view of the ordinary level of skill in the art.

Reconsideration of the Examiner's rejection is requested respectfully.

Summary of Applicants' Invention

Applicants' invention is summarized in the Reply to the Office Action dated October 22, 2003 which was filed February 23, 2004. In brief, it is emphasized herein that:

(A) the nature of the "all solids" dosage form defined in applicants' claim 1 permits advantageously drug formulations to be prepared by dry-blending techniques and direct compression of the blend to form a desirable dosage, for example, tablets, thus enabling the manufacturer of the dosage form to prepare it in an efficient and economic manner relative to dosage forms that include constituents that are in liquid or semi-solid state;

(B) applicants are the first to recognize that the enhancer compounds described in the present application (fatty acid-based enhancer), when used alone, are effective enhancers, that is, they provide for enhanced absorption of drugs from the gastrointestinal tract in the absence of other enhancers; and

(C) applicants are the first to recognize that the beneficial enhancing properties of applicants' fatty acid-based enhancers can be achieved by administering an "all solids" dosage form of the enhancer to sites of absorption in the gastrointestinal tract.

It should be emphasized also that preparation of dosage forms incorporating liquid or semi-solid constituents require specialized manufacturing equipment and specially trained personnel.

Examples and Figures hereof illustrate the preparation of tablet dosage forms by dry-blending techniques and direct compression into tablets; they illustrate also effective serum response in animals to which such tablets were administered orally in comparison with dosage forms lacking applicants' enhancer compounds (see the present application Example 2 (part "c"), as illustrated by the data in Figure 8, Example 3, as illustrated by the data in Figure 9, Example 5 (part "d"), as illustrated by the data in Figure 11, and Example 11, as illustrated by the data in Figure 14.

The disclosure of the Examiner's primary reference is summarized in the Reply filed February 23, 2004 to which the Examiner is referred.

Discussion of the Examiner's §102 Rejection of the "all solids" Embodiment

Applicants submit respectfully that the Examiner has failed to establish that the Watts publication anticipates applicants' "all-solids" embodiment; this embodiment is defined, for example, in claim 1, which definitively and unambiguously distinguishes over the reference in reciting that the dosage form and each of the constituents comprising the drug and enhancer composition is a solid at room temperature. The Watts publication does not disclose a composition comprising such solid constituents. The Watts publication discloses only liquid or semi-solid drug and enhancer compositions (see the Watts publication, page 8, line 21). The Examiner's attention is directed to Appendix A hereof which consists of pages 8 and 9 of the Watts publication and which spell out time after time that the compositions described therein are liquid or semi-solid.

In issuing the anticipatory rejection, the Examiner has violated a fundamental and basic principle of the law, that is:

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. (MPEP, Section 2131, page 2100-73, Rev. 2. May 2004).

The Examiner's anticipatory rejection is clearly not in compliance with the law in that the Examiner has not pointed out, and indeed cannot point out, where the aforementioned recitations are disclosed in the Watts publication. This is because they are not disclosed.

The Examiner's Action is revealing in that it includes statements that show that the Examiner is attempting to skirt around the appropriate application of the law respecting anticipation. This is evident from the Examiner's comments concerning applicants' previous traversal of the §102 rejection. The Examiner's present Action includes the following statement.

> One of ordinary skill in the art would know and hence would be able to select a solid or liquid as the starting constituent for making the composition. (paragraph 6. of the Action)

According to the law respecting anticipation, the issue is not what one skilled in the art would be led to do based on the disclosure of the reference, it is what in fact does the reference disclose. The aforementioned statement of the Examiner constitutes an acknowledgment that the Watts publication does not disclose a composition comprising ingredients all of which are solids at room temperature.

In the earlier Office Action of July 15, 2002, the Examiner took the position that the Watts publication discloses applicants' claimed "all solids" embodiment because the reference discloses that the Watts formulation can be in tablet or pellet form, each being a solid formulation. Watts teaches explicitly, however, that such tablets or pellets include liquid or semi-solid compositions which are micro-encapsulated prior to incorporation into a tablet or pellet dosage form (see the Watts publication, page 9, first complete paragraph). The previous paragraph of the Watts publication contains a detailed description of how to prepare the liquid/semi-solid filled capsules. Thus, it is abundantly clear that the Watts publication does not disclose a tablet or pellet or other dosage from which comprises a composition in which all of the ingredients are solids at room temperature, as set forth in applicants' claims.

In view of the above, it is requested respectfully that the Examiner withdraw the § 102 rejection asserted against applicants' "all solid" claims.

Discussion of the Examiner's § 103 Rejection of the "all solids" Claims

The Examiner's § 103 rejection is based also on the Watts publication; it is traversed for the following reasons.

The Examiner's Action states that the reasons for the § 103 rejection are those discussed in the previous Action, that is, the Action dated October 22, 2003. In that earlier Action, the Examiner states that applicants' "all solids" claims are *prima facie* obvious in view of the disclosure of the Watts publication. Applicants submit respectfully that the Examiner has not met the burden, as specified by law, for establishing a *prima facie* case of obviousness. Pursuant to the law, it must be shown that: (A) there is some suggestion or motivation, either in the cited documents themselves or in the knowledge of those skilled in the art, to modify or combine the cited disclosures; (B) there must be a reasonable expectation that the modification or combination of the cited disclosures would lead to a successful result; and (C) the combined disclosures must teach or suggest all of the elements of the claim (MPEP § 2143). All three of these requirements must be satisfied for the Examiner to establish a *prima facie* case of obviousness. If any one such requirement is not satisfied, then the Examiner must withdraw the rejection.

The prior art relied upon by the Examiner does not include any of the above showings. The Watts publication contains no suggestion or motivation that would lead one skilled in the art to modify its disclosure in a manner such that the compositions described in the Watts publication would wind up being comprised of ingredients, all of which are solids at room temperature. The Watts publication is concerned only with liquid/semi-solid compositions and the tablets and capsules described therein comprise, as stated explicitly by Watts, liquid/semi-solid compositions in encapsulated form. In addition, there is no evidence in the prior art that the modification proposed by the Examiner would lead to a successful result. Furthermore, there is no disclosure in the cited prior art that teaches or suggests that each and every one of the liquid/semi-solid ingredients comprising the Watts formulation should be discarded and replaced by an ingredient which is a solid at room temperature.

In fact, the Watts publication teaches directly against modifying the Watts composition in the manner proposed by the Examiner. This is evidenced by Example 4 of the

Watts publication. Example 4 describes a liquid composition prepared with caprylic acid (an 8-carbon liquid fatty acid) compared with a semi-solid composition prepared by substituting lauric acid (a 12-carbon solid acid) for caprylic acid. The Watts publication states that this example demonstrates that, as the Watts composition becomes increasingly viscous, the enhancement of drug absorption is decreased. (See Watts, page 19 at lines 25 to 29).

In the overall picture, it is abundantly clear that Watts, as one skilled in the art, considers his development to be one which for purposes of efficacy encompasses a liquid/semi-solid composition and in view of this consideration, there is no logical basis for anyone to convert the Watts development into being something that it is not. The Examiner, in attempting to do so, is not abiding by basic principles of law, as identified above, but is being motivated, not by any disclosure that appears in the Watts publication, but by disclosure that appears in the present application. Accordingly, it is requested respectfully that the Examiner withdraw the §103 rejection of the "all solids" claims.

<u>Discussion of the Examiner's §103 Rejection of the "fatty acid compound enhancer" Claims</u>

The Examiner states in the present Action that the §103 rejection of claims 53 to 66, based on the disclosure of the Watts publication, is asserted for the reasons set forth in the previous Action, that is, the Action dated October 22, 2003. In the previous Action, the Examiner rejected the involved claims as being *prima facie* obvious in view of the disclosure of the Watts publication.

It is submitted respectfully that the Examiner has not established a "*prima facie*" case of obviousness. Contrary to the law, as summarized above, the Examiner has not shown, with respect to the embodiment of claims 53 to 56, that: (A) there is some suggestion or motivation in the prior art to make the modification proposed by the Examiner; (B) there is a reasonable expectation that the modification would lead to a successful result; and (C) the disclosure teaches or suggests all elements of the claims.

Let it at once be understood that claims 53 to 66 define unambiguously that the <u>only enhancer</u> present in the claimed dosage form is a salt of a fatty acid (or one or more fatty acid enhancer compounds, as defined in claim 64) which has a carbon chain length of from 6 to 20

carbon atoms. The Watts publication describes the enhancer used in compositions described therein as comprising both an "absorption promoter" (for example, a fatty acid or salt thereof) and a "dispersing agent" (for example, a polyglycolized glyceride).

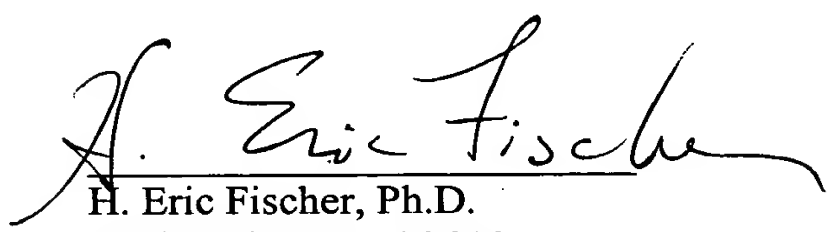
With respect to the *"prima facie"* requirement of (A) above, the primary reference (Watts) contains no disclosure which would motivate one skilled in the art to remove from the Watts composition the enhancer component comprising the dispersing agent and the Examiner has not identified any other prior art that would provide such motivation. Accordingly, the *"prima facie"* requirement of (A) above is not met.

With respect to the *"prima facie"* requirement of (B) above, the Watts publication contains definitive information that the modification suggested by the Examiner would lead not to a successful result, but to an unsuccessful result. The Watts publication discloses that, when used alone, neither the absorption promoter nor the dispersing agent is effective as an enhancer (see Watts page 13, lines 24 to 28). Thus, the Watts publication teaches explicitly that the modification suggested by the Examiner will not lead to success. And Watts' Example 3 illustrates this in that it shows that capric acid (a 10-carbon atom fatty acid), when used alone, is not effective as an enhancer in the Watts composition. It is abundantly clear thus the *"prima facie"* requirement of (B) above has not been met.

With respect to the *"prima facie"* requirement of (C) above, the above discussion concerning the prior art cited by the Examiner constitutes a sound and thorough explanation of why the cited prior art does not teach all of the elements of applicants' claims, but in fact teaches away from the modification proposed by the Examiner. Thus, the *"prima facie"* requirement of (C) above is not met. Accordingly, it is requested that the Examiner withdraw his §103 rejections of the "fatty acid compound enhancer" claims.

In view of the foregoing, applicants request respectfully that the Examiner allow the application in an early and favorable Action.

Respectfully submitted,
Synnestvedt & Lechner LLP



H. Eric Fischer, Ph.D.
Registration No. 46,010

August 4, 2004

Synnestvedt & Lechner LLP
2600 ARAMARK Tower
1101 Market Street
Philadelphia, PA 19107-2950
(215) 923-4466